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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,703	08/16/2004	Jean-Pierre Kinet	I00308/70002	2355

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WOLF GREENFIELD & SACKS, PC
FEDERAL RESERVE PLAZA
600 ATLANTIC AVENUE
BOSTON, MA 02210-2206

EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,703	KINET ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,16,21,24 and 29* is/are pending in the application.

4a) Of the above claim(s) *2,3,16,21 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-8 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/31/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response received January 25, 2006 is acknowledged.

Claims 9-15, 17-20, 22-23, 25-28, 30, and 31 were previously canceled.

Claims 1-8, 16, 21, 24, and 29 are pending in the instant application.

Applicant's election without traverse of Group II, claims 1, 4-8 and 24 as they read on methods of inhibiting FcεRI expression by administering polypeptides in the reply filed on January 25, 2006 is acknowledged.

Claims 2, 3, 16, 21, and 29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions. Election was made **without** traverse in the reply filed on January 25, 2006.

Applicant is respectfully requested to update the first line of the specification to indicate that the instant application is the national stage entry under 35 U.S.C. 371 of international application PCT/US00/25877 filed September 21, 2000 that claims priority to US provisional application 60/154,924, filed September 21, 1999.

Oath/Declaration

2. A review of applicant's declaration received August 16, 2004 appears to be complete. However, it is noted that on the page of the declaration signed by inventor Marie-Helene Jouvin her country of citizenship is listed as the United States. On the

pages that were not signed by Ms. Jouvin, her country of citizenship appears as France. The page signed by Ms. Jouvin controls, and as such her country of citizenship is the United States. If this discrepancy is a typographical error that occurred when the pages of the declaration were prepared and Ms. Jouvin is a French citizen, a new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date would be required. See MPEP §§ 602.01 and 602.02. Applicant is asked to verify the citizenship information and make appropriate corrections if they are required.

Information Disclosure Statement

3. Applicant's IDS received July 31, 2002 is acknowledged and has been considered.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 4-8, and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting expression of FcεRI by administering the polypeptide consisting of SEQ ID NO:4, does not reasonably provide enablement for a method of inhibiting FcεRI expression by administering the genus of FcεRIβ chain variant polypeptides. The specification does not enable any person skilled

in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's claimed method inhibits the expression of FcεRI by administering FcεRIβ chain variant polypeptides. FcεRI is made up of three distinct polypeptides, α, β, and γ, is the receptor for IgE, and crosslinking of this receptor leads to degranulation of mast cells and basophils in allergic responses (see particularly lines 15-31 of page 1 of the specification). Applicant provides data concerning a novel splice variant of the β chain (i.e. SEQ ID NO:4) which arises from the translation of an intron that is not spliced out, resulting in a truncated form that contains unique polypeptide sequence not found in the wild type polypeptide (see particularly lines 26-33 of page 19). Data provided by applicant in Examples 3-5 indicates that addition of this novel splice form to cells inhibits the proper assembly and expression of a functional FcεRI complex, and note that any method which inhibits FcεRI expression must inherently inhibit FcεRIα expression since this polypeptide chain is part of the receptor complex.

The breadth of the term FcεRIβ chain variant is defined by applicant as being the polypeptide of SEQ ID NO:4, the polynucleotide of SEQ ID NO:3 (which encodes SEQ ID NO:4) and structurally related polypeptides and polynucleotides that share a common function, specifically the ability to inhibit FcεRI expression (see from line 11 of page 8 to line 5 of page 10, most particularly the sentence that spans pages 8 and 9). Applicant defines structurally related polypeptides as being homologs and alleles that are at least 50 % identical to SEQ ID NO:4, (structurally related polynucleotides are 40% or more identical to SEQ ID NO:3) and also discloses that variants can be made by

mutagenesis and truncations of the wild type FcεRIβ chain sequence of SEQ ID NO:2 (see particularly lines 4-29 of page 9). Note that applicant's definition clearly indicates that an FcεRIβ chain variant nucleic acid is a variant because it encodes a polypeptide which would meet the definition of a FcεRIβ chain variant polypeptide based upon its polypeptide sequence alone (see the paragraph that spans pages 8 and 9, especially as it pertains to the term "dominant negative"). Applicant does not appear to provide any additional working examples concerning FcεRIβ chain variants other than SEQ ID NO:4, and the specification does not appear to provide guidance as to what residues or structures within SEQ ID NO:4 are required for its ability to inhibit FcεRI expression and therefore must be present in all variants, or conversely which residues are unimportant for this functional activity and can be altered at will.

Skolnick et al. teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (Trends in Biotechnology, 18(1):34-39, 2000, see entire document, particularly the abstract and the section titled Sequence-based approaches to function prediction on page 34). Even in situations where there is some confidence of a similar overall structure between two sequences, only experimental research can confirm the artisan's best guess as to the function of the structurally related sequence (see in particular the abstract and Box 2 on page 36 of Skolnick et al.). The complexity of the problem of assigning function based on homology rises as the percent similarity or identity falls (Whisstock et al., Quarterly Reviews of Biophysics, 2003, 36:307-340, see entire document, particularly the

sentence that spans pages 321 and 323).

Concerning SEQ ID NO:4, the specification discloses that this polypeptide lacks the C-terminal transmembrane and cytoplasmic domains as compared to the wild type sequence of FcεRIβ (see particularly lines 11-15 of page 29). SEQ ID NO:4 contains 16 amino acids that are not found in the wild type sequence, and applicant teaches that these residues may function as an imperfect transmembrane domain, or alternatively SEQ ID NO:4 may be topologically distinct from wild type FcεRIβ such that its C and N-termini are on opposite sides of the plasma membrane (see particularly lines 12-15 of page 29). Claim 5 indicated that the FcεRIβ chain variant to be administered comprises SEQ ID NO:4, and as such it contains additional sequence on either end of the polypeptide. This added sequence reasonably encompasses the addition of other polypeptide domains, including transmembrane domains. It is known in the art that the topological maturation of transmembrane proteins often shows unexpected levels of complexity wherein structural elements well separated in the primary amino acid sequence influence anterograde as well as retrograde translocation events to arrive at a mature topology that would not be predicted from simple analysis of the primary amino acid sequence, and that polypeptides with incorrect topology are non-functional (Lu et al., Molecular Biology of the Cell, 2000, 11:2973-2985, see entire document particularly the abstract, introduction, and the paragraph that spans pages 2983 and 2984). Given that interactions between the polypeptide subunits of FcεRI are critical for the assembly of a functional receptor and that these interactions take place because the polypeptides are in their correct orientation and spatial distribution in the membrane, the fact that

applicant does not know how the FcεRIβ chain variant of SEQ ID NO:4 is oriented in the membrane, and the teachings of the art that membrane orientation can be altered by sequences widely separated in the primary amino acid sequence in a way that is not readily predictable based upon the teachings of Lu et al., a skilled artisan would reasonably conclude that not all polypeptides comprising SEQ ID NO:4 have the same membrane topology as SEQ ID NO:4, that the precise topology of such polypeptides is unpredictable, and that if the membrane topology is not the same as SEQ ID NO:4 it may not share the function of SEQ ID NO:4 in inhibiting FcεRI expression.

Therefore, given that the specification does not appear to provide examples of FcεRIβ chain variants other than the polypeptide consisting of SEQ ID NO:4 and does not appear to provide guidance as to what sequences or structures are required to give rise to FcεRIβ chain variants which have the functional attribute of inhibiting FcεRI expression, the teachings of Skolnick et al. and Whisstock et al. concerning the unpredictability of assigning functional attributes to polypeptides of similar sequences in the absence of experimental data, the teachings of Lu et al. that the topology and function of transmembrane proteins can be influenced in an unpredictable way by the presence of sequences widely separated in the primary amino acid sequence, and the fact that applicant does not know the topology of SEQ ID NO:4 and has claimed the administration of polypeptides which comprise SEQ ID NO:4 and therefore contain additional amino acid sequence that can unpredictably alter membrane topology, a skilled artisan would not reasonably expect that the breadth of molecules defined by applicant as FcεRIβ chain variants, excepting the polypeptide consisting of SEQ ID

NO:4, would have the functional ability to inhibit FcεRI expression. As such, a skilled artisan would be unable to make and use the full breadth of applicant's claimed method without first conducting an undue amount additional research.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 4, 6-8, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Kinet (US Patent No. 5,770,396, see entire document).

Kinet teaches the wild type sequence of the human FcεRI beta chain (FcεRIβ) as well variants of the β chain (see entire document, particularly the abstract, lines 18-28 of column 2, lines 13-23 and 30-63 of column 9). The polypeptides of Kinet are taught for use as antagonists to prevent allergic responses when administered as therapeutic agents because they effectively inhibit the formation of FcεRI (see particularly lines 30-34 of column 2, lines 16-39 of column 10, and from line 62 of column 31 to line 21 of column 32). In addition to *in vivo* therapeutic use, the polypeptides of Kinet are also taught as being useful in drug screening methods and other *in vitro* assays (see particularly lines 21-39 of column 10 and from line 65 of column 28 to line 34 of column 32). Note that FcεRI is a tetrameric hetero-oligomer consisting of an α chain, a β chain

and two disulfide-linked γ chains (see lines 18-21 of column 2), and as such any method that inhibits expression of FcεRI must inhibit the expression of FcεRIα since FcεRIα is part of FcεRI.

Therefore, the prior art anticipates the claimed invention.

8. No claims are allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
March 31, 2006

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
4/12/06